REMARKS/ARGUMENTS

This application discloses pharmaceutical compositions comprising epothilones for use in the treatment of diseases of hyperproliferation. Particular embodiments of the invention include such pharmaceutical compositions comprising an epothilone, such as epothilone D or analogs or derivatives thereof, together with at least one cyclodextrin. Such epothilones generally have poor solubility in water, making therapeutic use difficult. As demonstrated in the working Examples, the application provides compositions having appropriate solubility properties for pharmaceutical use.

Claims 1-22 are pending in the application. In an Office Action mailed 13 September 2004, Examiner Michael C. Henry rejected Claims 1-22 on the grounds discussed below. Upon entry of this amendment, Claims 1, 4, 15, and 17 will be amended, and Claims 2 and 3 will be cancelled.

The Applicant respectfully requests that the Examiner consider the items in the Information Disclosure Statement submitted 15 November 2004 and initial and return the Form 1449 with the next Office Action.

Claim Objections

Claims 15-21 were objected to under 37 CFR 1.75(c) as being in improper form because a multiple dependent claim should not refer to other claims in the alternative only and/or cannot depend from any other multiple dependent claim. Claim 15 has been amended to be an independent claim, thus removing the multiple depency.

Claim 2 was objected to under 37 CFR 1.75(c) as being of improper dependent form for failing to further limit the subject matter of a previous claim. Claim 2 has been cancelled without prejudice, reserving the right to pursue claims of equivalent scope in subsequent timely filed continuation applications.

The Applicant respectfully requests that the Objections to the Claims be withdrawn.

Claim Rejections – 35 USC §102

Claims 1-8 and 22 stand rejected under 35 USC 120(b) as allegedly being anticipated by Hofmann *et al.*, US 6,194,181. The Hofmann reference discloses a method for the preparation of epothilones wherein cyclodextrins or cyclodextrin derivatives are added to fermentations of organisms that produce epothilones. The Examiner believes that the fermentation mixtures disclosed in the Hofmann reference anticipate the claims of the current application as the fermentation process comprises water together with an epothilone and a cyclodextrin.

The Applicant respectfully disagrees. Pharmaceutically acceptable carriers must be safe for administration to a patient. While sterile water-for-injection (WfI) is considered to be a pharmaceutically acceptable carrier, crude fermentation broths containing growing microorganisms together with their nutrients and by-products cannot be considered to be a pharmaceutically acceptable carrier, as they could not safely be administered to a patient in need of therapy. The Applicant therefore respectfully requests that this rejection be withdrawn.

Claim Rejections – 35 USC §103

Claims 9-14 stand rejected under 35 USC 103(a) as allegedly being unpatentable over the Hofmann reference. As described above, the Hofmann reference does not disclose or refer to pharmaceutical compositions comprising epothilones and cyclodextrins. Example 2A cited by the Examiner discloses the maximum concentrations of epothilones A and B obtained in fermentations upon addition of various cyclodextrins to the growing cultures of the producing microorganism. The Examiner states on page 5 of the Office Action:

> The difference between applicant's claimed composition and the composition of Hofmann et al. Is type of epothilone or the type of cyclodextrin claimed in the composition.

However, the Applicant respectfully submits that the difference between the claimed composition and the composition of the Hofmann reference is that the claimed compositions are pharmaceutical compositions, whereas those of the Hofmann reference are crude fermentation broths unsuited for pharmaceutical use. Given the unsuitable nature of the compositions of the Hofmann reference, one having ordinary skill in the pharmaceutical arts would not have been motivated to prepare the compositions of the Hofmann reference for use as an anticancer drug.

Similarly, one of ordinary skill in the pharmaceutical art would not be motivated to prepare the crude fermentation broth of the Hofmann reference in the form of a lyophilized composition.

Thus, the current claims are patentable over the Hofmann reference, and the Applicant respectfully requests that this rejection be withdrawn.

Other Amendments

Claim 1 has been amended to incorporate the limitation of Claim 3, and specify that the pharmaceutical composition comprises at least one cyclodextrin. Correspondingly, dependent Claim 3 has been cancelled, and the dependency of Claim 4 has been changed from Claim 3 to amended Claim 1. Support for this amendment is found in original Claim 3.

Claim 17 has been amended to correct the improper antecedent basis "polyene glycol" to "glycol." Support for this is found on page 6, first paragraph:

> As used herein, the term "glycol" is meant to include molecules such as propylene glycol, polyethylene glycol 400, polyoxyethylene sorbitan monooleate (sold under the trade name TWEEN 80), and related oxygenated hydrocarbons.

Summary

No new matter has been added. The Applicant respectfully requests entry of this Amendment, and withdrawal of all objections and rejections.

In the unlikely event that the transmittal letter is separated from this document and the Patent Office determines that an extension and/or other relief is required, Applicant petitions for any required relief including extensions of time and authorizes the Assistant Commissioner to charge the cost of such petitions and/or other fees due in connection with the filing of this document to **Deposit Account No. 50-2544** referencing docket no. 010072.02.

Respectfully submitted,

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By: _____

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